

In the Specification:

Please amend the specification as shown:

Please delete paragraph [0026] on pages 7-8, and replace it with the following paragraph:

[0026] Accordingly, RGD peptides useful as peptide and/or protein subunits include, but are not limited to, R R R R R R G D S P K (**SEQ ID NO: 17**), G(dR) G D S P A S S K, nMe G (dR) (dR)(dR)(dR) G G G (Dr) G D S P A S S K wherein R is the amino acid arginine; (Arg), dR is the amino acid D-arginine (D-Arg), G is the amino acid glycine (Gly), D is the amino acid aspartic acid (Asp), S is the amino acid serine (Ser), P is the amino acid proline (Pro), K is the amino acid lysine (Lys), A is the amino acid alanine (Ala) and nMe is a N-methyl group.

Please delete paragraph [0027] on page 8, and replace it with the following paragraph:

[0027] Other RGD or dRGD peptides or proteins useful as peptide and/or protein subunits include, but are not limited to, 1-Adamantaneacetyl-Cys-Gly-Arg-Gly-Asp-Ser-Pro-Cys [Disulfide bridge: 1-8] (**SEQ ID NO: 2**), Arg-Phe-Asp-Ser (**SEQ ID NO: 3**), Fibronectin Adhesion-promoting Peptide, Fibronectin Fragment 1377-1388, Fibronectin Fragment 1977-1991, Fibronectin Fragment III1-C recombinant expressed in *Escherichia coli*, Fibronectin Proteolytic Fragment human plasma, Fibronectin Proteolytic Grament human plasma, Fibronectin Proteolytic Grament human plasma, Fibronectin Type III Connecting Segment Fragment 90-109, Fibronectin Type III Connecting Segment Fragment 1-25, Gly-Arg-Gly-Asp

(SEQ ID NO: 4), Gly-Arg-Gly-Asp-Ser (SEQ ID NO: 5), Gly-Arg-Gly-Asp-Ser-Pro-Lys (SEQ ID NO: 6), Gly-Arg-Gly-Asp-Thr-Pro (SEQ ID NO: 7), Ser-Asp-Gly-Arg-Gly (SEQ ID NO: 8), N-Acetyl-Pen-Arg-Gly-Asp-Cys [Disulfide bridge: 1-5] (SEQ ID NO: 9), Arg-Gly-Asp, Arg-Gly-Asp-Ser (SEQ ID NO: 10), Arg-Gly-Asp-Ser-Pro-Ala-Ser-Ser-Lys-Pro (SEQ ID NO: 11), Arg-Gly-Glu-Ser (SEQ ID NO: 12) acetate salt, Cys-Asp-Pro-Gly-Tyr-Ile-Gly-Ser-Arg (SEQ ID NO: 13) and Cys-Ser-Arg-Ala-Arg-Lys-Gln-Ala-Ala-Ser-Ile-Lys-Val-Ala-Val-Ser-Ala-Asp-Arg (SEQ ID NO: 14). The above peptides are available from commercial suppliers

Please delete paragraph [0028] on page 8, and replace it with the following paragraph:

[0028] Some other RGD components useful as peptide and/or protein subunits in the present invention include, for example, Peptide 2000 from Telios Pharmaceuticals and GRGDSP (SEQ ID NO: 15) (Tweden *et al.*, *J. Heart Valve Dis.* **1995**, (Suppl. I): S90-97; Lateff *et al.*, *Biomaterials* **2002**, 3159-3168).

Please delete paragraph [0029] on pages 8-9, and replace it with the following paragraph:

[0029] YIGSR peptides (literal sequence disclosed as SEQ ID NO: 16) (e.g., Yamada *et al.*, United States Patent No. 5,039,885; Graf *et al.*, *Biochemistry* **1987**, 26, 6896) are also useful as peptide and/or protein subunits in the present invention. Exemplary YIGSR peptides (literal sequence disclosed as SEQ ID NO: 16) include, but are not limited to, Cys-Asp-Pro-Gly-Tyr-

Ile-Gly-Ser-Arg (CDPGYIGSR) (**SEQ ID NO: 13**) and pentapeptide Tyr-Ile-Gly-Ser-Arg (YIGSR) (**SEQ ID NO: 16**) (Massia *et al.*, *J Biol. Chem.* **1993**, 8053-9). Covalently immobilized laminin peptide Tyr-Ile-Gly-Ser-Arg (YIGSR) (**SEQ ID NO: 16**) supports cell spreading and co-localization of the 67-kilodalton laminin receptor with alpha-actinin and vinculin.

Please delete paragraph [0030] on page 9, and replace it with the following paragraph:

[0030] IKVAV peptides (**literal sequence disclosed as SEQ ID NO: 18**) (*e.g.*, Tashiro *et al.*, *J. Biol. Chem.* **1989**, 264, 16174; Jucker *et al.*, *J. Neurosci. Res.* **1987**, 26, 6896) are also useful as a peptide and/or protein subunit in the present invention. A preferred IKVAV (**literal sequence disclosed as SEQ ID NO: 18**) peptide is CYRARKQAASIKVAVSADR (SEQ ID NO:1) (Bellamkonda, United States Patent No. 5,834,029).

Please delete paragraph [0037] on page 11, and replace it with the following paragraph:

[0037] Bioactive polymers useful in practicing the current invention, include, but are not limited to, polymers where the peptide and/or protein subunit is an RGD peptide, IKVAV peptide (**SEQ ID NO: 18**), YISGR peptide (**SEQ ID NO: 19**), fibrin fragment or VEGF fragment. Also useful are polymers where the polysaccharide and/or proteoglycan subunit is heparan sulfate, chondroitin sulfate, keratan sulfate, perlecan or heparin. Other useful bioactive polymers

include, but are not limited to, polymers where the peptide and/or protein subunit is an RGD peptide, IKVAV peptide (**SEQ ID NO: 18**), YISGR peptide (**SEQ ID NO: 19**), fibrin fragment or VEGF fragment and the polysaccharide and/or proteoglycan subunit is heparan sulfate, chondroitin sulfate, keratan sulfate, perlecan or heparin. Particularly useful bioactive polymers include, but are not limited to, polymers comprised of heparin sulfate and a RGD peptide, chondroitin sulfate and a YISGR peptide (**SEQ ID NO: 19**), keratan sulfate and a VEGF fragment, a IKVAV peptide (**SEQ ID NO: 18**) and perlecan or heparin and a fibrin fragment.

Please delete paragraph [0047] on page 17, and replace it with the following paragraph:

[0047] The bioactive and biocompatible polymers may be combined non-covalently to form polymer blends and covalently to form interpenetrating polymer networks, copolymers and graft polymers. Preferred combinations of bioactive and biocompatible polymers include, but are not limited to, polyurethanes, heparan sulfate and RGD peptides, polyethylene oxides, chondroitin sulfate and YIGSR peptides (**literal sequence disclosed as SEQ ID NO: 16**), silicone polymers, keratan sulfate and VEGF biomimetic peptides, SIBS, perlecan and IKVAV peptides (**literal sequence disclosed as SEQ ID NO: 18**) and N-butyl methacrylate, heparin and fibrin fragments.

Please delete paragraph [0049] on page 18, and replace it with the following paragraph:

[0049] In one embodiment, a graft polymer is comprised of hyaluronic acid grafted to a copolymer of N-butyl methacrylate and glycidyl methacrylate. In another embodiment, the graft

polymer is comprised of an RGD peptide grafted to a copolymer of N-butyl methacrylate and glycidyl methacrylate. In still another embodiment, the graft polymer is comprised of an RGD peptide and hyaluronic acid grafted to a copolymer of N-butyl methacrylate and glycidyl methacrylate. Those of skill in the art will appreciate that a number of bioactive polymers, biocompatible polymers, RGD peptides, peptide and/or protein fragments, IVKAV peptides **(literal sequence disclosed as SEQ ID NO: 20)**, polysaccharides, polysaccharide fragments, *etc.* may be used to form graft polymers of the current invention.

Please delete paragraph [0050] on pages 18-19, and replace it with the following paragraph:

[0050] Graft polymers may be prepared by attaching the grafting agent to a preformed polymer. Thus, RGD peptides, peptide and/or protein fragments, IVKAV peptides **(literal sequence disclosed as SEQ ID NO: 20)**, polysaccharide, polysaccharide fragment, *etc.* may be attached to a preformed polymer by a variety of methods that will depend on the precise nature of the polymer and the grafting agent. For example, a polysaccharide or a peptide and/or protein fragment may be attached a carboxylic acid containing polymer by a variety of conventional methods, well known to those of skill in the art, used to form esters or amides.

Please delete paragraph [0056] on pages 20-21, and replace it with the following paragraph:

[0056] Interpenetrating polymer networks may be formed either sequentially or simultaneously, by methods known to the skilled artisan. The proteoglycan, *e.g.* heparin sulfate and the peptide, *e.g.*, GRGDSPS (**SEQ ID NO: 21**) may be linked using Schiff base chemistry or active ester (*e.g.*, carbodiimide) chemistry. An interpenetrating polymer network of the above bioactive polymer may be formed with a biocompatible polymer, (*e.g.*, a copolymer of butyl methacrylate and PEG) by using the method of Barber *et al.*, *J Biomed. Mater. Res.* **2003**, 38-47. Alternatively, during polymerization of a biocompatible polymer, *e.g.*, butyl methacrylate, the desired proteoglycans *e.g.*, heparin sulfate and peptide, *e.g.*, Peptide 2000, are suspended in the reaction mixture to provide an interpenetrating polymer network. Interpenetrating polymer networks may also be made by conventional methods known to those of skill in the art such as chemical crosslinking (Kosmala *et al.*, *Biomaterials* **2000**, 21, 2019-2023) and free radical polymerization including photopolymerization (Barber *et al.*, *J Biomed. Mater. Res.* **2003**, 54, 38-47; Elisseff *et al.*, *Plast. Reconstr. Surg.* **1999**, 104, 1014-1022; Hasciri *et al.*, *Biomed. Mater. Eng.* **2000**, 10, 19-29; Song *et al.*, *Electrophoresis* **2001**, 22, 3688-3698; Elisseff *et al.*, *J Biomed. Mater. Res.* **2000**, 51, 164-171). For example, during polymerization of a biocompatible polymer, *e.g.*, butyl methacrylate, the desired proteoglycan *e.g.*, heparin sulfate and peptide, *e.g.*, Peptide 2000, are suspended in the reaction mixture to provide an interpenetrating polymer network. Interpenetrating polymer networks may also be prepared by methods including melt blending, solution blending or other methods known to the skilled artisan.

Please delete paragraph [0057] on page 21, and replace it with the following paragraph:

[0057] A biocompatible polymer with a reactive group can provide for graft polymerization of a bioactive polymer to provide a biomaterial of the current invention. One preferred copolymer is a copolymer of butyl methacrylate and PEG containing a primary amine based on aminoethyl methacrylate. A preferred proteoglycan, *e.g.*, heparan sulfate can be grafted to the biocompatible polymer, post copolymerization *via*, for example, carbodiimide chemistry. The peptide, *e.g.*, an RGD peptide such as GRGDSP (**SEQ ID NO: 15**) can be grafted to PEG by any number of methods, *e.g.*, using Schiff base chemistry and glutaraldehyde. Other methods include similar linking chemistries (*e.g.*, carbodiimide, difunctional linkers like glutaraldehyde) with any hydroxy, amino, thio, isocyanate or other “active hydrogen” functional group polymer.

Please delete paragraph [0071] on page 27, and replace it with the following paragraph:

[0071] The peptide GGGRGDGGG (**SEQ ID NO: 22**) which is made either by New England Peptide Co., Gardner MA or Biopeptide Co., LLC, San Diego, CA is dissolved in a water-miscible solvent. The peptide solution is then dissolved in conjugation buffer (0.1 M MES buffer at pH of 4.7 2-20mg per 2 mL) and is added to the polymer prepared in Example 3. Conjugation buffer (0.5 mL) is added to EDC and to the EDC solution is added to the above reaction mixture (EDC to peptide ratio = 1:1). The reaction mixture is shaken gently for three

hours and the EDC solution removed. The polymer product is washed with distilled water three times.